



NIA ADC Clinical Task Force UDS Neuropsychology Work Group March 2013

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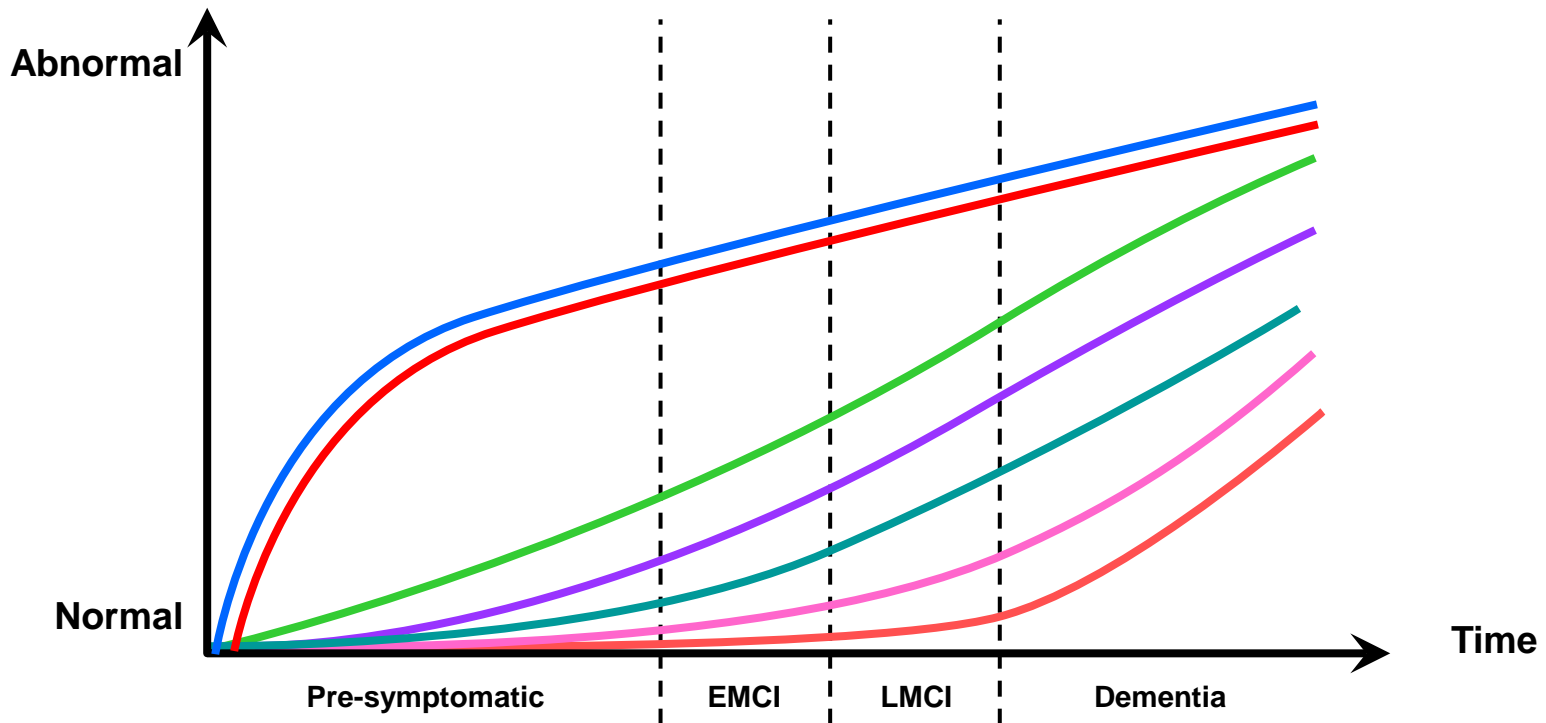
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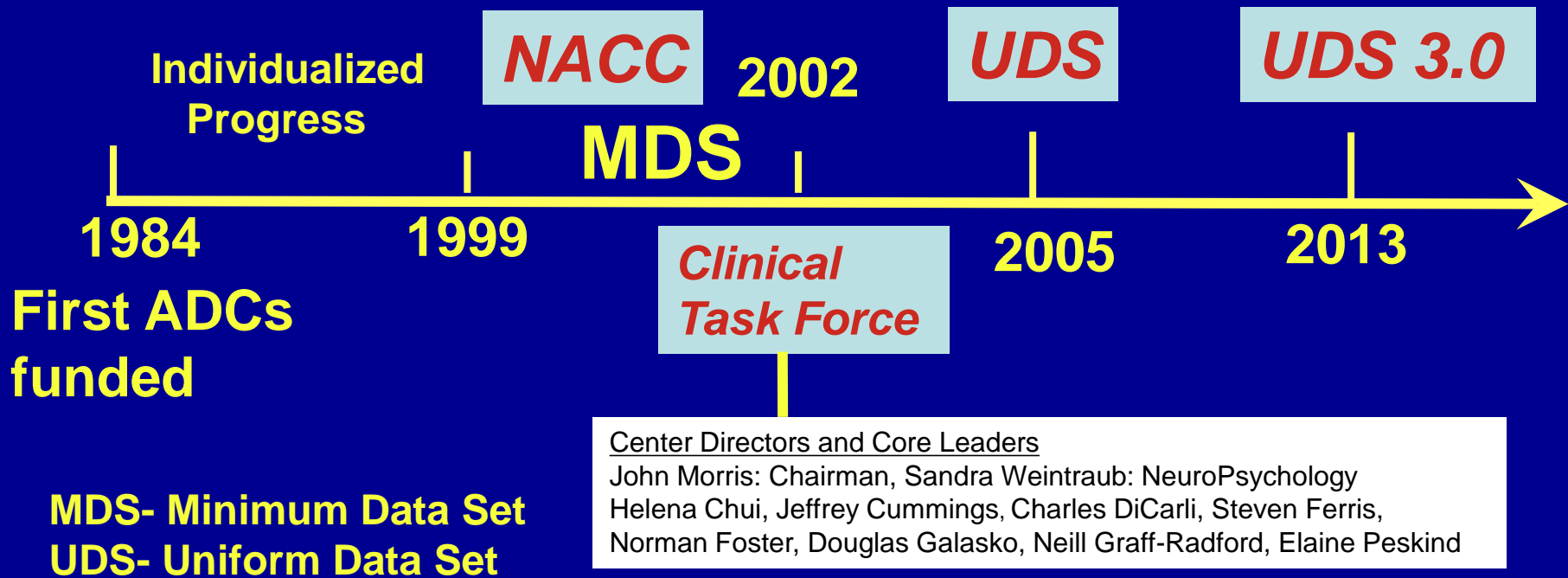
Hypothetical Model of Biomarkers



Jack et al, 2010



Milestones in the NIA ADC data collection program





Cognitive Assessment Increasingly Important in Identifying Signs of Decline and Endpoints for Treatment

- **For the purpose of the UDS, a set of common cognitive data elements is important to leverage the efforts of the centers on large numbers of participants**
- **Allows for comparisons across centers and for multi center initiatives**
- **MDS was too minimal but how much is just right?**



WHY CHANGE?

- **CONTROL OF BATTERY USAGE:** Collaborators must now obtain independent license agreements to use some tests in the UDS Neuropsychological Battery
- **COSTS:** Costs keep escalating on current tests

WHY SWAP AND NOT SWITCH?

- **LEGACY DATA:** Battery is short and replacement of tests with similar instruments was judged more advantageous than introducing an entirely new battery
- **WHAT ABOUT COMPUTERIZED TESTS?** UDS committee has considered some options as a next step



Work Group Recommendations

Drop: Digit Symbol

Keep: Trail Making A and B
Fluency Animals and Vegetables

Replace: MMSE → MoCA

Digit Span → Number Span

BNT → MINT

Logical Memory → Craft Story 21

Add: Benson Complex Figure Test (Copy and Recall)-part of FTLD Module



Computerized Tests

- Shelved proposal to compare CogState and Toolbox (Collab)
- If we want to combine computer tests from different measures, will need further consideration (EXAMINER, NIHTB, Other)
- Need instruments that have biomarker validity (e.g., Face-Name test)
- Will the computer tests replace or add to paper-and-pencil battery?



PROGRESS

- **NACC DATA FORMS:** Number Span; Craft Story 21 (Immediate and Delayed); MINT; Benson Complex Figure (Part of FTLD Module) Immediate and Delayed; MoCA
- **Cross-Walk Study Plan:** Administer 4 new and old tests to new and return visit participants. Require N=30* of each: AD, MCI, NC. Once established, new enrolls get new battery, old can continue with old battery until death or dropout; *need to determine who will pay for license agreements and for how long*
- **Collection of letters of agreement from test designers:** (Nasreddine-MoCA; Kramer: Number Span and Benson Complex Figure; Craft: Story 21; Gollan: MINT)

** rough estimate: actual number required depends more on variations in the data received*



CROSSWALK OPTIONS

	Strengths	Weaknesses
At least half of the Centers participate, all subjects, all tests)	<ul style="list-style-type: none"> -faster subject accrual -less complicated -more varied sample -guarantee both initial (needed to avoid retesting effects) and follow-up visits -more feedback from Centers on testing length, scoring difficulties, etc. 	<ul style="list-style-type: none"> -may come off as burdensome to Centers -may end up sampling more subjects than necessary
Opt-in plan (Centers volunteer to participate, give one test, not all subjects included)	<ul style="list-style-type: none"> -more palatable to Centers -centers not moving to the new battery for a year or two will not have to train staff -performing and scoring fewer tests could reduce visit length and speed up data entry 	<ul style="list-style-type: none"> -sample may not be useful since selected artificially -will not be able to track expected data that hasn't been entered (delayed entry) -no way of predicting completion date (rate of submission will vary over time) -will take more time to complete study



CRAFT STORY 21

Maria's / child / Ricky / played / soccer / every Monday / at 3:30. /
He / liked / going / to the field / behind / their / house / and joining /
the game. / One / day, / he / kicked / the ball / so / hard / that it /
went / over / the neighbor's / fence / where three / large / dogs /
lived. / The dogs' / owner / heard / loud / barking, / came / out, /
and helped / them / retrieve / the ball

Total story units recalled (VERBATIM SCORING): / 44

Total story units recalled (PARAPHRASE SCORING): / 25

Craft S, Newcomer J, Kanne S, Dagogo-Jack S, Cryer P, Sheline Y, Luby J, Dagogo-Jack A, Alderson A. Memory improvement following induced hyperinsulinemia in Alzheimer's disease. *Neurobiol Aging*. 1996 Jan-Feb;17(1):123-30.



SELECTED MINT ITEMS

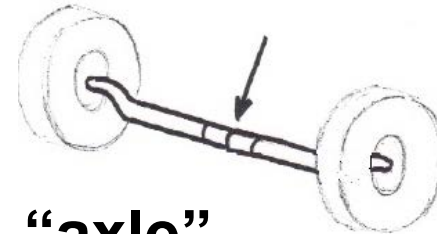


“candle”



“parachute”

“wig”



“axle”

Ivanova I, Salmon DP, Gollan TH. The Multilingual Naming Test in Alzheimer's Disease: Clues to the Origin of Naming Impairments. J Int Neuropsychol Soc. 2013 Jan 8:1-12.

Gollan TH, Weissburger G, Runnqvist E, Montoya RI, Cera CM. Self-ratings of spoken language dominance: A Multilingual Naming Test (MINT) and preliminary norms for young and aging Spanish–English bilinguals. Bilingualism: Language and Cognition. 2011;13:215-8.



- 3. **MoCA — Total score (0–30)** _____
- 3a. **Visuospatial/executive (0–5)** _____
- 3b. **Naming (0–3)** _____
- 3c. **Attention: List of digits (0–2)** _____
- 3d. **Attention: List of letters (0–1)** _____
- 3e. **Attention: Serial 7 subtraction (0–3)** _____
- 3f. **Language: Repeat (0–2)** _____
- 3g. **Language: Fluency (0–1)** _____
- 3h. **Abstraction (0–2)** _____
- 3i. **Delayed recall (0–5)** _____
- 3j. **Orientation (0–6)** _____

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Estimated Accrual if 50% of Centers Participate

	3 months	6 months
IV packets	196	390
FV packets	848	1700
Total	1044	290

** rough estimate: actual number required depends more on variations in the data received*

Monsell et al



Estimated Accrual in 3 Months if 50% Participation by CDR Code

	CDR=0	CDR=0.5	CDR=1	CDR>1	Total
IV packets	63	82	43	8	196
FV packets	431	228	113	76	848
Total	494	310	156	84	1044

** rough estimate: actual number required depends more on variations in the data received*

Monseil et al



CONCERNS

- Replacing current with similar tests allows continuity with legacy data but does not address the need for more forward-looking measures (biomarker validated; preclinical detection)
- Burden on centers/participants to collect cross-walk data



OTHER ISSUES

- Many centers collect word list measures.

5 CVLT; 1 CVLT-II; 14 CERAD; 6 RAVLT;
5 ADAS-COG; 3 HVLT(1R); 3 FCSRT; 3 Other
- Might it be possible/feasible to enter word-list data centers already collect to NACC database ***provided methods are the same across centers for the same test?***



NEXT

- **DISCUSSION**-options; gradually phase out current UDS; new UDS can serve to follow beyond pre-clinical stages; develop more pre-clinical tests
- **TIME LINE:** Cross walk study data collection to be initiated and well on its way by next directors' meeting?